RECEIVED
DEC - 2
VET. MED. LIBRARY

O STATE
UNIVERSITY
DEC - 2 1959

The Veterinary Record

PATRON: HER MAJESTY THE QUEEN

Vol. 71 No. 38 Issue No. 4250 797-818

BROADER CONTROL

OF SKIN DISORDERS IN CATS AND DOGS

VIOFORM (iodochlorhydroxyquinoline) is a powerful antiseptic. It has practical advantages over antibiotics and sulphonamides. It does not produce resistant strains or side effects.

In Dogs and Cats, non-parasitic skin disorders — especially when complicated by secondary bacterial or fungal infection — usually respond quickly to the application of VIOFORM in combination with hydrocortisone.

VIOFORM—HYDROCORTISONE SALVE

VIOFORM-HYDROCORTISONE SALVE effectively controls both inflammation and infection.

It is soothing, rapidly relieves itching and encourages healing.

Due to its high potency, only small amounts need be applied. Application once or twice daily is usually adequate.

Available in 5 G. Tubes each containing:

Vioform	3%
Hydrocortisone	1%

in an emollient greasy base.

CIBA

CIBA LABORATORIES LIMITED, HORSHAM, SUSSEX

The
VETERINARY RECORD

Founded by William Hunting, F.R.C.V.S., in 1888
7, MANSFIELD STREET, PORTLAND PLACE, LONDON, W.1. MUSEUM 6541

No. 38 NOVEMBER 7th, 1959 Vol. 71

Registered for Transmission as a Newspaper *Price 2s. post free*

Parenteral Administration of Copper Compounds to Cattle with Special Reference to Copper Glycine (Copper Amino-acetate)

BY

RUTH ALLCROFT

Ministry of Agriculture, Fisheries and Food, Central Veterinary Laboratory, Weybridge, Surrey

AND

OLGA UVAROV

Glaxo Laboratories Ltd., Greenford, Middlesex

SUMMARY.—A large number of copper compounds were investigated on laboratory animals. Only 3 appeared to be suitable for use in cattle. Further tests showed that of these only copper glycine was satisfactory. Detailed observations were made after intramuscular and subcutaneous injections into various sites. Normal and copper-deficient animals of several age groups were used over a period of 2 years.

General results and conclusions were:—

1. *Considerable variation in reactions occurred in different animals. The intramuscular route was considered unsuitable, particularly in beef animals. The subcutaneous route using the brisket site was satisfactory.*

2. *Absorption into the liver was good by subcutaneous and intramuscular routes, but in general was better with the former.*

3. *Differences in uptake of copper by the liver were found to be related to the initial copper status of the animal and to the type of feeding.*

4. *The duration of increased copper storage was shown to depend on the severity of the factor in the herbage inducing the deficiency, so that no specific times of injection could be suggested. In general 2 to 3 injections a year should control copper deficiency symptoms even under severe conditions.*

5. *Injecting the dam with copper glycine about 1 to 4 months before calving increased the copper content of the new-born calf's liver.*

6. *Repeated injections of multiple doses of copper glycine, supplying a total of 3,600 mg. Cu, to 3 cows over a 7-month period produced no toxic effects and indicated that parenteral administration of this preparation of copper glycine had a wide margin of safety for cattle.*

Introduction

COPPER deficiency in cattle and sheep occurs in many parts of the world and is associated with considerable differences of copper concentration in the herbage. When the content is low—usually under 5 parts per million (p.p.m.) in dry matter (D.M.)—and when factors interfering with efficient utilisation or metabolism, or both, are, or appear to be, absent or minimal, the condition may be economically controlled by top-dressing pastures with 5 to 10 lb. of copper sulphate per acre. This increases the level to about 10 p.p.m. (D.M.)—a value regarded as normal and sufficient to correct the deficiency in the animals.

In Britain, however, and in other parts of the world, where a "conditioned" or "induced" deficiency occurs in cattle and sheep on pastures containing apparently adequate or even high concentrations of copper, ranging from 13 to 37 p.p.m. (Allcroft & Lewis, 1957), top-dressing with copper sulphate is not always a satisfactory method of control.

Unpublished work by Jamieson and Allcroft (1951)

has shown that an application of 10 lb. copper sulphate per acre to pastures in Caithness increased the copper content of some from about 11 p.p.m. to about 15 p.p.m. for a period of several months, though in other pastures no increase in copper content was observed. Similar findings were reported by Morgan and Clegg (1958) after top-dressing pastures in Lancashire.

The Caithness observations also showed that top-dressing controlled symptoms of "copper pine" in calves over a 5-months' grazing period on fields in which an increase in copper content of the pasture did occur or where extraneous copper sulphate remained on the herbage for about 2 months, owing to low rainfall. In the following season, however, pining recurred when cows and calves grazed the same pastures not retreated with copper sulphate. Field (1957) also found this method effective over one grazing season.

In Great Britain top-dressing is not used to any extent, owing to the cost of labour, the need for annual applications, the lack of increase in the copper concentration of the pasture, and in particular because of the risk to sheep of copper poisoning on farms where both sheep and cattle are kept.

Various other methods of administration of copper supplements, usually as copper sulphate, are used: they include systematic dosing by drenching, offering licks or mineral mixtures containing copper, incorporation of copper sulphate in concentrate mixtures, application as a solution on the concentrates, addition to the drinking water. All these methods have disadvantages, for sheep and for grazing cattle generally and particularly for young stock and store animals that are not handled at frequent intervals and do not receive concentrate rations.

The effectiveness of parenteral administration of copper was demonstrated by Allcroft (1947) and reported by Green (1949). An intravenous injection of 300 mg. of copper, as a solution of copper sulphate in physiological saline, was shown to maintain normal blood copper levels and to control scouring in cattle grazing "teart" pastures in Somerset. Later work (Jamieson & Allcroft, 1950) showed that 50 mg. of copper as a similar solution given intravenously controlled pining in calves in Caithness. This method of administration has since been frequently used for experimental and clinical purposes, but has many limitations, in particular that of the time and care required for giving the injections to large numbers of animals.

Harvey and Sutherland (1953) reported the results of subcutaneous and intramuscular injection of various copper compounds into ruminants. Thirteen compounds were tried; of these an aqueous solution of copper glycine (copper amino-acetate) administered subcutaneously to sheep appeared to be the most satisfactory. It produced only slight local damage, it was quickly absorbed and stored, and the margin of safety between therapeutic and toxic doses was adequate.

Cunningham (1957) showed that copper glycine mixed with a sterile base of neatsfoot oil-marrow fat, or beeswax-peanut oil, was a suitable source of copper for subcutaneous or intramuscular administration to cattle and sheep in New Zealand. This was confirmed by Allcroft (1957), who used a slightly different base.

The purpose of the work reported here was to find a copper compound that would (i) give as good absorption of copper as that obtained from copper sulphate given intravenously, (ii) cause a minimum amount of irritation at the site of injection, (iii) have a low toxicity and a wide margin of safety, and (iv) be easily administered under field conditions. A description is given of the local and systemic reactions and degree of absorption after parenteral administration of several different copper compounds to large numbers of cattle.

Experimental Procedure

Animals. Preliminary screening of more than 80 different copper compounds was carried out on small laboratory animals. Clinical assessment of suitable compounds was made on cattle of all ages, from 1-month-old calves to 8- to 9-year-old cows. Some of these were stalled; others were at grass: they included lactating, dry and young stock of either low or normal copper status. In all 174 animals were used, many of them being given repeated injections at different times and by different routes.

Method of Administration

(a) *Subcutaneous:* (1) in front of the brisket, *i.e.* into the loose folds of the dewlap; (2) into various areas over the ribs and in the flanks.

(b) *Intramuscular:* (1) in the hind quarter, into either the gluteal or the biceps femoris and semitendinosus muscles; (2) in the fore quarter into the triceps and supraspinatous muscles; (3) in the neck into the trapezius muscle.

(c) *Intravenous:* into the jugular vein by means of a flutter valve.

The site for injection was normally prepared by clipping the hair and disinfecting the area. A few injections were purposely made without clipping or disinfection, though with sterilised needles.

Assessment of Reactions

Sites of injections were examined by palpation, and any swellings were measured. Daily observations were made on some animals for the first 10 days, after which less frequent examinations at twice weekly or weekly intervals were found to be sufficient. Temperatures were at first recorded, but it was found that there was no deviation from the normal, even at the height of the reaction, and this check was therefore discontinued.

Some animals were killed at different intervals after injection for *post-mortem* examination. Histological examination of the tissues at the site of injection was made from a number of them. Most of the animals were kept under observation for 1 to 2 years after injection.

Assessment of Absorption and Storage of Copper

Since the liver is the main storage depot for copper, absorption was measured by the increase in concentration of liver copper after injection. This was determined by taking pre- and post-injection liver

biopsy samples at intervals ranging from 2 to 28 days after injection. Duration of storage was measured by taking samples at longer intervals. Effectiveness of absorption was at first assessed by comparison with that obtained from the intravenous injection of a solution of copper sulphate supplying a similar dose of copper. When sufficient information was obtained on absorption from the different preparations, the intravenous route was discontinued, since our primary purpose was to find a substance that could be easily injected under field conditions.

All concentrations of liver copper have been expressed on a dry matter basis, which is the conventional method in use. This may have the effect of suggesting that in some animals (calves and young stock) the increase has been greater than the amount of copper injected. For example, in Fig. 5 it appears that increases of 240 and 195 p.p.m. were obtained 7 days after intravenous or subcutaneous injection of 120 mg. copper. The average dry matter content of liver is 25 per cent., so that on a wet matter or *in vivo* basis the increases would be only of the order of 60 and 50 p.p.m. respectively.

Transference of copper to the foetus was assessed in a few pregnant animals by injecting the cows at intervals before calving and killing the calves 1 to 4 days after birth. The liver copper concentration of the calf was compared with those of new-born calves from uninjected cows in the same herd kept under similar conditions. Blood copper levels were determined in a number of animals before and at various intervals after injection. In a group of 12 lactating cows the copper concentrations of the milk were determined before and after injection of copper glycine. In 2 herds of 20 and 60 animals respectively, routine monthly blood samples were taken for determinations of copper, calcium, magnesium, inorganic phosphorus, and haemoglobin. Since the only significant variations relating to the injections occurred in the blood copper levels, the results for the other constituents are not reported.

Copper Compounds and Vehicles Used

1. *A standard copper glycine product* in a tube*—similar to that already reported by Cunningham—was incorporated in a base consisting of arachis oil and beeswax gel contained in single-dose tubes delivering 120 mg. copper as copper glycine in a total volume of about 1.2 ml. The tubes were fitted with a record mount and the contents were squeezed through a 17 gauge needle, which was found to be the most satisfactory size.

2. *Diluted copper glycine.* The concentrations of copper glycine in arachis oil with aluminium monosterate gel used were 60, 120, and 240 mg. copper per 10 ml. Doses of 10 ml. of all these dilutions and 5 ml. of 240 mg. per 10 ml. were injected; the subcutaneous route only was used for this preparation.

3. *Copper calcium ethylenediamine tetra-acetic acid complex.* A suspension of this complex was prepared in a mixture of aluminium monosterate and arachis oil so that 1 ml. contained 40 mg. copper. This was injected subcutaneously or intramuscularly.

4. *Copper sulphate solution.* For intravenous injection a solution of copper sulphate containing 7.85 g. $CuSo_4 \cdot 5H_2O$ and 8.5 g. NaCl in 1 litre distilled water was used. This gives a concentration of 1 mg. Cu per ml.

Vehicles

The different vehicles used for the copper compounds were themselves injected subcutaneously and intramuscularly into 24 animals. There were no visible or palpable reactions during the subsequent 2-week period of close observation or later.

* Copper "120" Injection, Glaxo.

Results

Copper Glycine

Since this was ultimately found to be the most satisfactory of the preparations investigated, more extensive observations were made on reactions and absorption after injection of copper glycine than on the effects of the other two copper compounds tried on cattle. All ages and types of animals were used, including both stalled and grazing animals, as well as a dairy herd kept under ordinary commercial farming conditions.

1. Reactions

Subcutaneous Route

(i) *Brisket site.* This was used in 139 animals. In all of them some degree of swelling occurred and reached a maximum by the fourth to fifth day after injection. The swellings were hard, though apparently not painful, and seemed to cause no inconvenience to the animals even when the reaction was severe. The size of the reaction varied greatly among the animals. In general, those of calves were smaller than those of adult animals. Various degrees of reaction are shown in Figs. 1 and 2. Measurements ranged from 4 × 3 inches to about 14 × 14 inches and the greatest was an exception measuring 26 × 37 inches. In lactating animals no losses of milk were noted. As a rule the swellings subsided within 3 to 5 weeks after injection, but sometimes a small, invisible, though palpable, fibrous nodule persisted for a few weeks longer. In most animals no reaction could be detected 4 to 6 months after injection.

(ii) *Ribs and flanks.* Sites over these areas and behind the shoulder were used in 13 animals. The resulting extensive oedematous swellings were painful to the touch and at times extended over the entire area of the rib and flank to the mid-line of the belly. Because of this pronounced and painful reaction, these sites were not used for subsequent injections.

Intramuscular Route

(i) *Neck region.* Injections of 1 or 2 doses of the standard product supplying 120 mg. or 240 mg. copper were made into the trapezius muscles of 12 animals. No visible or palpable reactions occurred, but 2 animals appeared to have some stiffness in the neck, which persisted in one for about a week.

(ii) *Fore quarter.* No abnormality could be detected after injections in this region.

(iii) *Hind quarter.* Seventy-two injections were made into the specified muscles of this region. In

most instances no palpable reaction could be observed. In a few animals fairly extensive fluid swellings occurred in the gluteal region, but subsided within 2 to 3 weeks to a slight induration. One

FIG. 1.—Reactions in calves 5 days after subcutaneous injection of 120 mg. Cu as copper glycine into the brisket site. Calves left to right: (1) control; (2) moderate reaction; (3) severe reaction.

FIG. 2.—Reactions in milking cows after subcutaneous injection of 120 mg. Cu as copper glycine into the brisket site. Cows left to right: (1) control; (2) slight reaction; (3) severe reaction.

animal retained a reaction approximately the size of an orange. Serous fluid withdrawn from two such oedematous swellings was sterile. There was no lameness in any of these animals.

Other experiments were carried out to see if 2 standard doses (2 × 120 mg.) of copper glycine injected at the same site would materially alter the size and severity of reactions. On the whole the double doses produced somewhat larger swellings, although considerable variation occurred between animals.

Post-mortem Examination

On *post-mortem* examination 3 days to 8 months after injection, reactions were observed having various degrees of severity, depending on the interval between injection and slaughter.

1. *Subcutaneous injection.* In animals killed 3 days after injection the area surrounding the injection site was necrotic and oedematous, with some early granulation. In animals killed at longer intervals after injection (4 to 8 months), no detectable lesions could be found in most of those examined.

2. *Intramuscular injection.* (a) *Fore and hind quarters.* In all muscles some degree of fibrosis was found. Inspissated cysts ranging from $\frac{1}{4} \times \frac{1}{4}$ inch to 5 × 3 inches were detected in some animals. In animals killed up to 2 weeks after injection some cysts were hard and caseous; others contained necrotic and liquefied material, but bacteriological examinations of them gave negative results.

Animals that had been injected 9 months before slaughter showed smaller areas of fibrosis and cyst formation: some of these were difficult to detect; in others inspissated pus and caseous material was still present.

(b) *Neck region.* In only 1 out of 8 animals was a lesion detected on *post-mortem* examination. It consisted of a small inspissated cyst that showed on microscopical examination an area of necrosis with some reparative response.

Microscopical Examination

In the relatively few muscles examined the severity of the lesions depended upon the interval between injection and slaughter. Three days after injection necrosis and oedema and at times abscess formation were seen. Only slight evidence of reparative response was noted. Fibrosis surrounded by normal tissue could be observed in a few muscles only.

In animals killed 53 days after injection some necrotic tisue could at times be detected. Dense interstitial fibrosis was often present, particularly in areas adjacent to cysts. In other muscles no necrosis could be found, and a reparative response was evident. In view of these reactions, although in most instances they could not be detected by clinical examination, use of the intramuscular route was discontinued.

2. Absorption of Copper

Some of the animals used were copper deficient, others were of normal copper status before injection, so that there was a wide variation in pre-injection liver copper levels. The increases in liver copper concentration obtained by administration of various compounds by different routes were recorded by histograms showing the mean increases obtained at different times after injection.

Rapidity of Uptake by the Liver

In a small preliminary experiment on six 12- to 18-month-old cattle, housed and on stall rations, the rapidity of copper absorption by the liver after subcutaneous or intramuscular injection of 120 mg. of copper, as copper glycine, was compared with that after intravenous injection of a solution of copper sulphate supplying the same amount of copper. Two animals were used for each route of administration; liver biopsy samples were taken before injection and at 2, 6, and 14 days afterwards.

The increases in liver copper concentrations are shown in Fig. 3.

The number of animals was admittedly small, but the results clearly indicate that increase in storage of

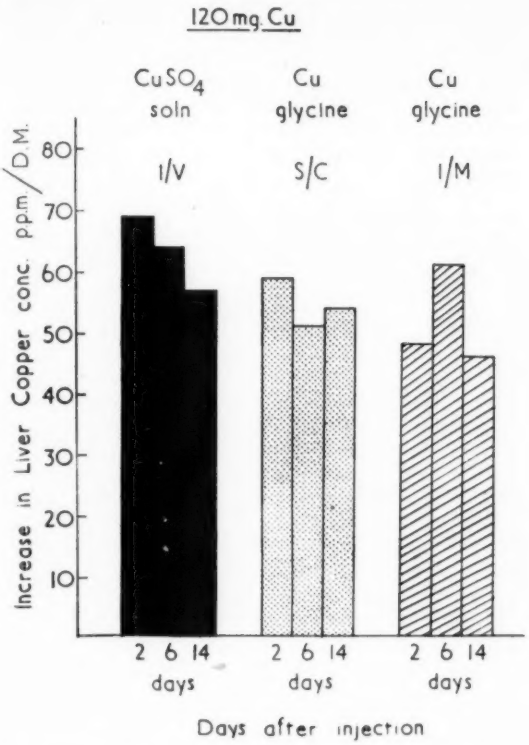

FIG. 3.—Increase in concentration of liver copper in normal 12- to 18-month-old cattle after parenteral administration of 120 mg. Cu as copper sulphate or copper glycine by the routes indicated.

copper by the liver after either subcutaneous or intramuscular injection of copper glycine was of the same order as that due to intravenous injection of copper sulphate solution. At 2 days, the increase after intravenous injection appeared to be greatest, as would be expected, but there was little difference between the 3 groups, after 14 days.

Comparison of Absorption after Different Routes of Administration to Normal and Copper-deficient Animals

Normal

(a) *Adult cows.* One standard dose of copper glycine (120 mg. Cu) was given to each of 32 grazing Ayrshire dairy cows of normal copper status. Half were injected subcutaneously in the brisket site and the other half intramuscularly in the hindquarter, into either the gluteal or the biceps femoris. Another 6 stalled animals were given the same amount of copper intravenously as a copper sulphate solution. Liver biopsy samples were taken before injection and at 6 and 21 days afterwards. The results are shown in Fig. 4. It is evident that at 6 days after intravenous injection, liver copper concentrations were much greater in the 6 stalled cattle than in the 2 younger animals, injected intravenously, in the previous experiment (Fig. 3). The reason for this

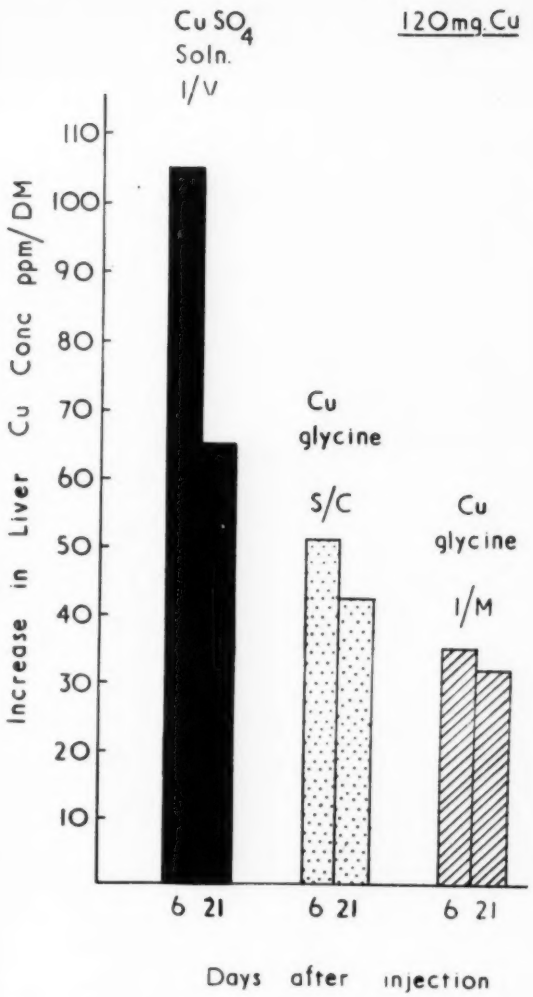

FIG. 4.—Increase in concentration of liver copper in normal adult dairy cows after parenteral administration of 120 mg. Cu as copper sulphate or copper glycine by the routes indicated.

seems to have been individual variability. However, even though absorption was greater, the fall in concentration was much more rapid between 6 and 21 days after intravenous injection than after either subcutaneous or intramuscular injection. When allowance is made for the difference in age, and therefore in size of liver, between these adult cows and the younger animals used previously (Fig. 3), absorption after subcutaneous injection was of the same order. It is apparent, however, that the increase obtained was significantly less after intramuscular than after subcutaneous injection, the mean increase at 6 days being only 35 p.p.m. copper after the former compared with 51 p.p.m. after the latter. After 21 days there was a slight fall in liver copper concentration, and although this was more marked in the sub-

cutaneous group, the mean values were still higher than in the intramuscular group.

(b) *Calves.* Nine of a group of fourteen 4- to 8-month-old Ayrshire stalled calves of normal copper status (mean liver Cu 100 p.p.m. (D.M.)) were given one standard dose of copper glycine (120 mg. Cu) subcutaneously at the brisket site; the other 5 were given the same amount of copper intravenously as a solution of copper sulphate. The increases in liver copper concentration at 7 and 21 days after injection are shown in Fig. 5. Absorption obtained by the subcutaneous route compared favourably with that by the intravenous route. No intramuscular injections were given to this group of calves, since by the time this experiment was carried out enough information was already available to indicate that the intramuscular was less suitable than the subcutaneous route.

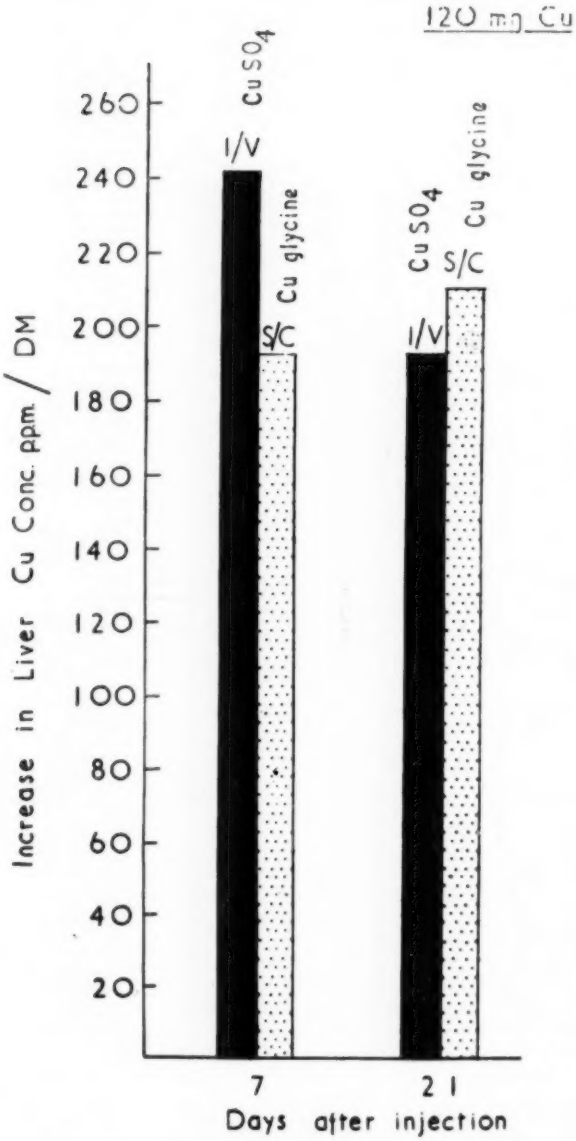

FIG. 5.—Increase in concentration of liver copper in normal 4- to 8-month-old stalled calves after injection of 120 mg. Cu as copper sulphate and copper glycine by the routes indicated.

Copper-deficient Animals

Studies were made on animals of various age groups in an Ayrshire herd of about 60 animals on a farm where severe copper deficiency occurred. Calves born with a normal copper status remained normal while housed and fed on the usual rearing rations, but soon became copper deficient after being turned out to grass.

The liver copper values on biopsy samples from 56 animals before administration of copper averaged 5.4 p.p.m., the range being from 2 to 16 p.p.m. (D.M.).

For these investigations the milking herd of 24 cows and their followers of various ages were divided into 3 approximately equal groups. One group was left untreated and allowed to remain deficient in copper, a second was given a solution of copper sulphate intravenously, and the third was injected either subcutaneously or intramuscularly with the standard preparation of copper glycine. Doses of 120, 240, and to a few animals 480 mg. copper were given. When the subcutaneous route was used, 240 mg. copper (2 tubes of the standard preparation) were injected into the same site. When the intramuscular route was used, not more than 240 mg. copper (2 tubes) was injected into the same site and to some animals 120 mg. copper (1 tube) were given at 1 to 4 different sites.

Ages ranged from calves 3 to 4 months old to cows 8 years old; injections were given at all stages of pregnancy, up to 2 days before parturition in 4 animals. Absorption of copper into the liver was estimated from liver biopsy samples taken 3 to 4 weeks after injection; it was not possible to take samples at more frequent intervals in this herd.

(a) *Adult stock.* The results for animals from about 2 years upwards in age are given in Fig. 6.

Comparison with Figs. 3 and 4 shows that the increase in liver copper concentration after injecting 120 mg. copper by any of the 3 routes used was less in this copper deficient herd than in the animals of normal copper status. After a dose of 120 mg. copper, absorption was similar by both subcutaneous and intramuscular routes; after a dose of 240 mg. copper, absorption by the subcutaneous route was again greater than by the intramuscular route. Increases in liver copper concentration were approximately proportional to the dose after intravenous and subcutaneous, but not after intramuscular injection.

A dose of 480 mg. (4 tubes) was given intramuscularly to 4 animals at two different sites: its absorption was compared with that from intravenous injection of a similar dose. The subcutaneous route was not used for this large dose, since it was considered inadvisable to give more than 2 doses into the brisket site.

It should be pointed out that the high dose of

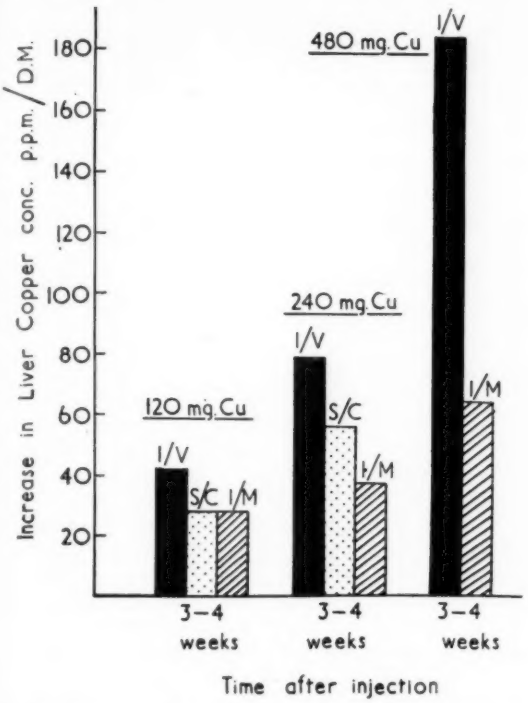

FIG. 6.—Increase in concentration of liver copper in copper-deficient adult cattle at grass after administration of 120 mg., 240 mg., and 480 mg. Cu as copper sulphate or copper glycine by the routes indicated.

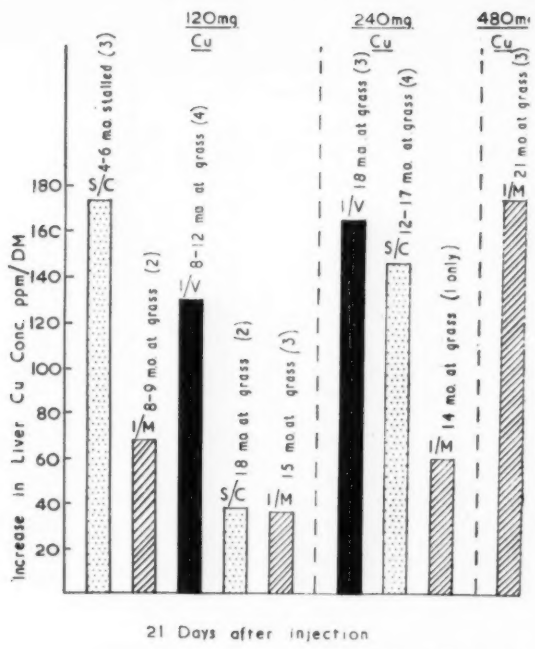

FIG. 7.—Increase in concentration of liver copper in copper-deficient young stock of various ages after administration of 120 mg., 240 mg., and 480 mg. Cu as copper sulphate or copper glycine by the routes indicated. The figures in brackets indicate the number of animals in each age group.

480 mg. copper given intravenously is not without danger and was given only for experimental purposes; one of the animals in this group died the day after injection, showing shock and subsequent collapse. Although the liver copper concentration was only 150 p.p.m., it is difficult not to relate death to the intravenous injection of the large dose of copper sulphate given on the previous day. Reports have been received (personal communications) of several other instances in which death has occurred in cattle receiving intravenous injections of copper sulphate solution in large doses, yet without the symptoms usually found in chronic copper poisoning and with only a slight increase of copper in the liver.

(b) *Young stock.* It was not possible to compare the three routes of administration in all age groups of the young stock. In Fig. 7 the increases in liver copper concentrations are shown for small groups of animals from about 4 to 18 months of age after administration of 120, 240, and 480 mg. Cu as copper glycine subcutaneously or intramuscularly and of copper sulphate intravenously.

All these animals had a low copper status (liver copper < 20 p.p.m. (D.M.)) before injection, except the housed 4- to 6-month-old calves whose pre-injection mean value for liver copper was 148 p.p.m.

Because of the small numbers in these groups, the increases in concentration of liver copper can only be regarded as an indication of the absorption due to injection of various doses by different routes, rather than as a clear pattern such as was shown by some of the previous results. When doses of 120 mg. Cu were used, the substantial increase obtained after subcutaneous injection in the three 4- to 6-month-old housed calves was of the same order as by the same route in the 4- to 8-month-old housed calves (Fig. 5): the copper status of both groups was normal before injection. In the remaining young stock, which were at grass and had average liver copper values of less than 12 p.p.m. before injection, absorption was rather less than expected after injection by each of the three routes, when compared with results obtained from the adult cattle in this herd (Fig. 6), even if allowance is made for difference in ages.

When doses of 240 mg. Cu were used, absorption of copper into the liver was better from the subcutaneous than from the intramuscular injections. After doses of 480 mg. Cu given intramuscularly to three 21-month-old animals, the increase was relatively greater (Fig. 7) than was obtained from the same dose injected intramuscularly into adult cattle in this herd (Fig. 6).

In general, the increases obtained in all age groups indicate that in a herd showing severe copper deficiency, doses supplying as much as 240 mg. copper may be necessary to increase liver copper concentration to adequate levels.

3. Duration of Effect of Injected Copper

Some idea of the length of time for which the liver

TABLE I
DURATION OF EFFECT OF INJECTED COPPER
MEAN LIVER AND BLOOD COPPER CONCENTRATIONS (WITH STANDARD DEVIATIONS) EXPRESSED AS p.p.m. (D.M.) AND mg/100 ml. RESPECTIVELY

Number of animals	Cu compound, route of injection, and amount of Cu given	Before injection		After injection					
				3 weeks		4 months		8 months	
		Liver	Blood	Liver	Blood	Liver	Blood	Liver	Blood
	(a) Copper deficient cattle at grass								
12	Controls No Cu	4·5 (±2·12)	0·028 (±0·006)	5·7 (±1·75)	0·025 (±0·0097)	5·3 (±1·79)	0·039 (±0·016)	5·3 (±2·82)	0·036 (±0·0093)
4	Copper 480 mg. Cu	6·4	0·040	190	0·080	79	0·100	13·1	0·085
7	sulphate 240 ,, ,,	5·0	0·035	136	0·093	44	0·090	4·4	0·073
6	soln. i/v 120 ,, ,,	6·8	0·043	106	0·092	23	0·098	3·9	0·070
		(±3·19)	(±0·013)	(±57·8)	(±0·016)	(±22·6)	(±0·016)	(±6·14)	(±0·015)
7	Copper 480 mg. Cu	5·0	0·034	115	0·086	56	0·100	4·5	0·087
6	glycine 240 ,, ,,	4·9	0·042	70	0·085	35	0·078	8·8	0·093
4	i/m 120 ,, ,,	5·7	0·050	47	0·087	13	0·070	4·9	0·100
		(±1·84)	(±0·014)	(±67·8)	(±0·012)	(±12·0)	(±0·021)	(±3·52)	(±0·012)
2	Copper 240 mg. Cu	6·2	0·035	58	0·085	—	—	4·6	0·040
8	glycine 120 ,, ,,	12·5	0·070	42	0·088	—	—	4·6	0·035
	s/c	(±6·37)	(±0·025	(±8·94)	(±0·012)	—	—	(±1·66)	(±0·007)
	(b) Stalled cattle of normal copper status								
3	Copper 240 mg. Cu	64·3	0·097	153	0·106	183	0·110	233	0·110
	glycine Range :	(49–86)	(0·09–	(130–	(0·10–	(150–	(0·10–	(190–	(0·10–
	i/m		0·10)	170)	0·11)	220)	0·12)	300)	0·12)

and blood copper concentrations remained above the pre-injection levels was obtained from the herd in which severe copper deficiency occurred. Liver biopsy and blood samples were taken before administration of copper and at 3 weeks, 4 months, and 8 months after injection; a group of 12 untreated animals acted as controls. Previous observations had shown that severe copper deficiency occurred in cattle on this farm and that intravenous injections of copper sulphate solution had to be given at intervals of about 6 months to maintain even "low normal" concentrations of liver copper. The duration of effect of intramuscular or subcutaneous injections of copper glycine were therefore compared with that of intravenous copper sulphate. For comparison, similar observations were made on 3 stalled animals of normal copper status fed on a hay and concentrate ration.

The results are given in Table I and show that liver copper values were higher 4 months after injection in the intravenously injected group than in the other two, but since absorption was better in the former, this would have been expected. However, 8 months after injection the liver copper concentrations of all 3 groups were in the deficiency range.

Comparison of the rate of fall in liver copper concentration after intravenous or intramuscular injection of 240 mg. copper showed that it was greater with the former treatment than with the latter, the fall per week being of the order of 6 p.p.m. in animals given intravenous copper sulphate and 3 p.p.m. in animals given intramuscular copper glycine. This suggests that the liver absorbs copper more readily after intravenous injection of copper sulphate, but may also lose it more readily, perhaps because of the difference between the copper compounds used.

The increase in blood copper levels after administering copper by the three routes is also shown in Table I. The levels of the groups given copper intravenously and intramuscularly were still within the "normal" range (above 0.06 mg. per 100 ml.) at 8 months, even though concentrations in the liver copper were low. A lack of correlation between blood and liver copper levels was reported by Loosmore & Allcroft (1951), and Cunningham (1946) observed that a fall in blood copper levels could be retarded by provision of copper from the liver reserves.

The mean increase in liver copper in the 3 stalled animals of normal copper status was somewhat higher than that obtained from injecting the copper deficient animals with an equal dose by the same route, but no depletion occurred subsequently. In fact, the animals continued to store copper. The copper content of their rations was similar to, but certainly no higher than, that of the herbage grazed by the copper deficient herd, the range being about 15 to 30 p.p.m. for both. A marked increase of blood copper values in copper deficient animals transferred from pasture to stall rations of similar copper content was reported by Allcroft & Parker (1949); later observations (Allcroft & Lewis, 1954) have confirmed that a concomitant increase in liver copper concentration also occurs on stall rations providing an adequate copper intake.

4. Transfer of Copper to Foetus

During 1957 and 1958 an Ayrshire herd in which copper deficiency occurred was used to study the effect of parenterally administered copper to the dam and its subsequent transfer to the foetus.

Bull calves born to cows injected with copper sulphate or copper glycine about 1 to 4 months before parturition were killed within 4 days of birth

TABLE II
EFFECT OF COPPER INJECTED DURING PREGNANCY ON THE COPPER STATUS OF RESULTANT NEW-BORN CALVES

Number of calves	Copper compound, route and amount of Cu given to dam	Number of days between injection of dam and birth of calf	Liver Cu conc. of dam p.p.m. (D.M.)	Liver Cu concentration of calf p.p.m. (D.M.)	
				Range	Mean
4	Copper sulphate solution i/v — 300 mg. Cu	26—38	—	110—220	168
2	Copper sulphate solution i/v — 240 mg. Cu	46—65	—	290—350	320
1	Copper sulphate solution i/v — 120 mg. Cu	54	60 (34 days*)		210
2	Copper glycine i/m — 240 mg. Cu	122—124	5—8 (2—5 days*)	200—270	235
1	Copper glycine i/m — 120 mg. Cu	44	16 (26 days*)		330
1	Copper glycine s/c — 120 mg. Cu	44	25 (24 days*)		340
12	Controls—no Cu given	—	2—11 (mean 5·2)	5—100	47

* Number of days before calving when biopsy samples were obtained.

and their liver copper values were compared with those of bull calves from control cows. Concentrations of liver copper were determined in a number of cows 2 to 34 days *pre-partum*.

The results given in Table II show that, even when allowance is made for the variations in liver copper content between individuals and for the different time intervals between injection and calving, parenteral administration of copper to the dam significantly increased the concentrations of liver copper in the new-born calf. From these limited data it appears that there is no quantitative relationship between the amount of copper administered to the dam and the copper concentration in the neonatal calf liver. Nor do the results suggest any relationship between increase in the calf's concentration of liver copper and the route of administration or the type of copper compound used.

These results agree with those of Field (1957), who showed that calves born to cows given 10 g. of $CuSO_4$ orally at fortnightly intervals during pregnancy had higher copper levels in their liver than those of calves from untreated cows deficient in copper. These levels also showed no quantitative relationship with the amounts of copper given to the cows during pregnancy, and the range of values was wider than that of the figures now reported (Table II).

The results shown in Table II also indicate that copper concentration in the dam's liver falls during gestation. This is in agreement with observations of van der Grift (1955), who showed that the amount of copper in the liver of pregnant cows decreased during the last 4 months of pregnancy.

There appears to be little correlation between maternal and foetal concentrations of liver copper during the last week or two of pregnancy, since values of only 5 to 8 p.p.m. were found 2 and 5 days before calving in 2 cows that had been given 240 mg. copper about 4 months previously, and whose calves had liver copper values of 200 and 270 p.p.m. respectively. These maternal values for liver copper were of the same order as those found in the untreated cows whose liver copper levels remained consistently low and within the range 2 to 11 p.p.m. throughout 12 months that included the period of pregnancy, whereas the levels of liver copper in the 2 treated cows had been 40 to 50 p.p.m. about 3 months previously. This indicates that administration of copper to the dam during the last 4 months of pregnancy permits enhanced transference of copper to the foetus even though the maternal liver copper reserves may be depleted in the process.

5. Effect of Copper Glycine Injections on Concentrations of Copper in Milk, Blood, and Liver of Cows of Normal Copper Status

From our previous knowledge about oral or intravenous administration of copper to cattle of normal copper status, it appeared unlikely that subcutaneous or intramuscular injection of copper glycine to such animals would have any significant effect on milk and blood copper levels. To verify this, 12 milking cows were divided into 3 equal groups.

Groups I and II were given 1 standard dose of copper glycine (120 mg. Cu) by the intramuscular and subcutaneous routes, respectively: group III served as controls. Morning milk samples were taken from all 12 cows on 4 consecutive days and blood samples on 2 days before injection. Post-injection morning milk and blood samples were taken at 1-, 3-, 7-, and 14-day intervals. Liver biopsy samples were taken before injection and 14 days afterwards.

Table III shows the mean copper values for milk, blood, and liver samples, before and after administration of copper glycine. Each mean value represents the mean of all pre- and post-injection samples in all 4 animals in the group; the range of individual values is also given.

Milk copper values were all extremely low, 68 per cent. of these being less than 0.01 mg. per 100 ml.; they showed only slight differences from group to group and between pre-injection and post-injection samples.

The range of blood copper values was also small; although there appeared to be a slight rise in the

TABLE III
EFFECT OF COPPER GLYCINE INJECTIONS ON CONCENTRATIONS OF COPPER IN MILK, BLOOD AND LIVER OF COWS OF NORMAL COPPER STATUS

Group. 4 animals in each group	Number of samples/ animal :	Milk copper mg./100 ml.		Blood copper mg./100 ml.		Liver copper p.p.m. (D.M.)	
		Pre-injection 4	Post-injection 4	Pre-injection 2	Post-injection 4	Pre-injection 1	Post-injection 1
I i/m	Mean	0·0088*	0·0078	0·098	0·103	85	125
	Range	<0·01–0·03	<0·01–0·02	0·09–0·11	0·09–0·11	36–160	81–210
	Mean difference	−0·0010		+0·005		+40	
II s/c	Mean	0·0081	0·0088	0·094	0·101	61	118
	Range	<0·01–0·02	<0·01–0·02	0·08–0·10	0·08–0·12	33–110	51–210
	Mean difference	+0·0007		+0·007		+57	
III Control	Mean	0·0106	0·0053	0·103	0·096	51	57
	Range	<0·01–0·03	<0·01–0·01	0·08–0·12	0·08–0·10	33–77	32–95
	Mean difference	−0·0053		−0·007		+6	

Milk copper *Values of <0·01 are taken as 0·005 for calculation of means.
Blood copper Standard error = 0·0084.
Liver copper Standard error of differences between pre- and post-injection samples = 8·68.

means of groups I and II after injection of copper, the differences were not significant. The standard error taken over all blood copper estimations was 0.0084, and there would have to be a difference of 0.017 (*i.e.* twice the standard error) between pre- and post-injection means to have statistical significance at a value of $P = 0.05$.

Routine blood samples were taken from these animals over a period of 2 years; no significant increase in blood copper levels that could be associated with the injection of copper glycine was subsequently noted. This agrees with results obtained from administering small oral supplements of copper to cattle of normal copper status.

Figures for liver copper from each animal showed greater variation within the groups than the milk and blood values, both before and after copper was given, but all animals in groups I and II showed a marked increase after injection. The standard error of the differences between pre- and post-injection was 8.68; therefore a mean increase exceeding 26.9 in any group would be highly significant (t for $P_{0.01} = 3.1$), so that the increases in groups I and II were highly significant, while those in group III were not, the mean difference being only 6. The increase after subcutaneous injection was greater than that after intramuscular injection, but owing to the small number of animals in each group, the difference was not quite significant.

6. Toxicity of Copper Glycine

The possibility that repeated injections of copper glycine might have toxic effects was also investigated. Thirty standard doses, supplying a total of 3,600 mg. copper, were given intramuscularly over a 7-month period to 3 adult cows, Y, L, and 3641, of which No. 3641 was pregnant. All were housed and fed on stall rations throughout. Multiple doses were given on each occasion; at first 2×120 mg. doses were given and after that 4 × 120 mg. doses at each time of injection, usually into 4 different sites, though sometimes 2 doses were injected into the same site. Liver biopsy samples were taken at intervals, usually of 1 to 2 weeks, after each administration; blood copper levels were also checked at intervals. The last injections of 4 × 120 mg. doses were given 5 months after the beginning of the experiment. One cow (No. 3641) calved 2 months later. All 3 animals were killed 3½ months after the last injection, and the tissues at the sites of injections were examined.

At the beginning of this experiment, copper concentrations in the livers of all 3 animals were similar, Y, L, and 3641 having values of 200, 220, and 200 p.p.m. (D.M.), respectively. The dates on which injections were given and the liver biopsy samples taken are indicated in Fig. 8, which shows the increases obtained in concentration of liver copper. Since the values for cows Y and L were of the same order throughout the experimental period, the mean values for these 2 animals are compared with the values for cow 3641.

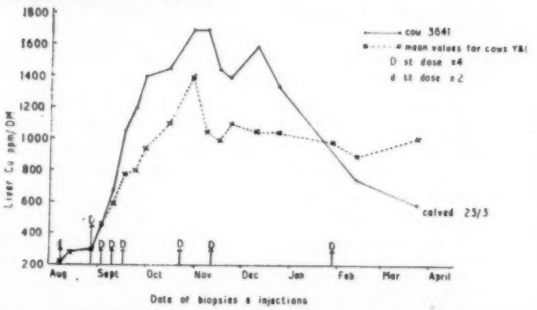

FIG. 8.—Increase in concentration of liver copper after repeated intramuscular injections of copper glycine into 3 cows over a period of 7 months. D and d indicate times at which injections were given: points × and · indicate times at which liver biopsy samples were taken.

There were no symptoms of toxicity throughout the nine months during which these animals were under close observation.

It is evident that the accumulation of liver copper was greatest during the first 3 to 4 months, after which there was a fall in concentration in spite of further injections. Between the second and fifth

months, higher concentrations were always present in the pregnant cow No. 3641. In cows Y and L, it appeared as though the liver was incapable of further absorption once the peak level of 1,400 p.p.m. (D.M.) had been reached a week after 2,640 mg. of copper had been given (October 22nd, 1957, see Fig. 8). The reason for the fall in liver copper level to 1,050 p.p.m., which occurred in these 2 animals a week after this peak level, is not known. After injection of another 4 × 120 mg. doses on November 11th, a further slight fall of 50 p.p.m. occurred and then a small increase of 100 p.p.m. to a level of 1,100 p.p.m. It was thought that absorption might be delayed owing to reservoirs of copper glycine in cysts formed at sites of injection: 5 liver biopsy samples were therefore taken over the next 6 weeks, during which no further injections were given. Not only was liver copper concentration not significantly increased during this period, but a further small decrease occurred about 2 weeks after the last injection of 4 × 120 mg. doses on January 28th, 1958, and before the final slight increase to 1,020 p.p.m.

The marked fall in liver copper occurring in the pregnant cow No. 3641 from December 9th, 1957, until calving on March 23rd, 1958, is understandable, since it is known that the concentration of liver copper falls throughout gestation (van der Grift, 1955). Such a rapid and marked fall was, however, unexpected, as was the lack of any increase after the last injection of 4 × 120 mg. doses on January 28th, 1958. The concentration of liver copper in the calf 2 days after birth was 290 p.p.m., which was lower than was here expected. The calf appeared to be normal in all respects.

The relatively limited accumulation of copper in the livers of these 3 animals after administration of frequently repeated and large doses of copper glycine was unexpected. The results, together with the absence of any toxic symptoms, indicate that this compound has a wide margin of safety in the bovine animal.

Dilute Copper Glycine

Suspensions of this were used to find out if the dilution caused less irritation to the tissues at the site of injection and if absorption of copper was as good as from the more concentrated standard tube product. It was hoped that, if the reaction were less and absorption as good, such a diluted suspension might have advantages when larger doses than those provided by the tubes were required. Subcutaneous injections in the brisket or rib areas were made on 26 lactating and dry cows and 18 young stock aged 4 to 24 months, including animals of normal and low copper status.

The milking cows were given one injection into the brisket site of 10 ml. of a suspension containing 240 mg. Cu. The other animals received 5- or 10-ml. injections of this suspension, the calves being given 5 ml. (120 mg. Cu) doses, whereas the older animals were given either 1 × 10 ml. (240 mg. Cu), 2 × 5 ml. (240 mg. Cu), or 2 × 10 ml. (480 mg. Cu) doses in the brisket or rib areas or in both. One month after these injections some animals, but not the milking cows, were given another injection of 10 ml. of a suspension containing either 60 or 120 mg. Cu per 10 ml.

Reactions

Local reactions from the various dilutions of copper glycine varied considerably. For instance, in some young stock and adults 60 mg. copper glycine per 10 ml. produced severe, and at times painful, reactions, whereas in others no pain could be detected and reactions were not more severe than from the standard preparation.

The highest dilution (60 mg. Cu per 10 ml.) did not modify the resultant swelling, although there was considerable variation between animals. This applied particularly to some stalled animals for which chain fastenings were used: moreover the swellings on occasions appeared to be painful and took considerably longer to subside; some burst, discharging oil and unabsorbed copper. It appeared that friction due to the chain fastenings aggravated the reaction. Since dilution of copper glycine did not reduce its irritant effect, the diluted material was considered unsuitable for replacing the standard product.

Absorption

One liver biopsy sample, or more than one, was taken from most of these animals at intervals of 7, 8, 11, 15, 21, or 28 days after injection. Comparison of the results with those obtained after injecting the standard product of copper glycine showed that absorption was much more variable. In grazing and lactating cows of normal and low copper status, a dose of the diluted product supplying 240 mg. Cu gave increases in concentrations of liver copper of the same order as were obtained from only half that dose of the standard preparation. Satisfactory mean increases of 90 and 104 p.p.m. (D.M.) at 8 and 21 days respectively after injection were obtained from the same dose (240 mg. Cu) given to stalled dry cows; 4- to 8-month-old calves also showed a good mean increase of 153 p.p.m. seven days after injection of 5 ml. doses supplying 120 mg. Cu.

When more dilute suspensions containing only 60 or 120 mg. Cu per 10 ml. were used to re-inject 2 groups of 5 animals one month later, the mean increase in liver copper 11 days after injection was approximately the same in both groups, *viz.* 80 p.p.m. It is possible that the unexpectedly large increase in the group receiving only 60 mg. Cu may have been due to continued and delayed absorption from the injections of 240 or 480 mg. Cu given to these animals a month earlier. However, in view of the pronounced and painful swellings, together with the marked variability of absorption in some animals, it was decided that this diluted copper glycine preparation was not worth further investigation.

Copper Calcium Ethylenediamine Tetra-acetic Acid Complex

This preparation produced no local reactions in rabbits and their absorption of copper from it was satisfactory. However, when injected into 27 cattle

by the subcutaneous or intramuscular routes, severe local reactions, which were also painful, occurred in 17. Moreover, the swellings were slow to subside and sometimes persisted for many weeks.

Absorption

Doses of 3 or 6 ml. of this compound supplying 120 or 240 mg. copper were given subcutaneously or intramuscularly to 13 milking cows, 9 dry cows, and five 4- to 8-month-old calves, all of normal copper status. Absorption was similar and satisfactory by either route in the milking cows and calves. Increases of about 80 p.p.m. and 150 p.p.m. were obtained in the cows 7 days after injection of doses supplying 120 and 240 mg. copper, respectively, and were of the same order in the calves when allowance is made for difference in size of liver relative to dose.

Absorption was not satisfactory by either intramuscular or subcutaneous route in 9 dry cows, no increase being obtained in 5 and a slight increase only in the other 4 cows at 2 and 8 days after injection. Further re-injection of 6 ml. (240 mg. Cu) resulted in only a slight increase in 4 animals 2½ weeks later. Owing to this variation in absorption of copper and to the fact that it produced pronounced and persistent local reactions which were often painful, and also because it was a difficult preparation to handle, it was decided that it would not be of any use under field conditions and therefore no further experiments were done with this material.

Discussion

The widespread occurrence of copper deficiency throughout the country is well known. Fig. 9 gives (from data collected at Weybridge over a number of years) some indication of its distribution in cattle. Although several methods of control have been in use for some time, Cunningham (1957) has recently shown that the parenteral administration of copper amino-acetate has advantages over other forms of therapy under some field conditions.

The results now presented confirm in many respects Cunningham's reports (1957a and b), which described the satisfactory use of copper glycinate mixed with a neatsfoot oil and marrow fat or beeswax and peanut oil base for parenteral administration to cattle and sheep. He observed that resultant local reactions to subcutaneous injections varied and depended on the base used, being about 50 per cent. greater and more persistent with the beeswax and peanut oil formulation; in the main, reactions subsided 21 to 36 days after injection. Although he noted no local reaction of any importance after injection of the bases alone, a small patch of fibrous tissue was frequently found. In our investigations a different base (arachis oil and beeswax gel) was used; when injected alone it was non-irritant and did not produce reactions. However, reactions from injection of this copper glycine preparation appeared to be, on the whole, more severe than those described by Cunningham, but they subsided about the same time. Painful reactions resulted only when subcutaneous injections were given in the area over the ribs. The brisket site is therefore preferred. Cunningham's findings also indicated that absorption of copper was better from the brisket than from the rib area.

FIG. 9.—Areas where copper deficiency in cattle has been found. The large shaded areas were intensively investigated and most herds were found to be affected.

Although Cunningham (1957a) made detailed observations on only 25 yearling cattle, its use in some 500 cattle in field experiments led him to conclude that the subcutaneous route was preferable in beef cattle even though a noticeable reaction frequently occurred; any fibrous nodule that might persist could easily be trimmed off at slaughter without damage to hide or carcase. His objection to the intramuscular route for meat animals was because of the occasional formation of a cold abscess, which would escape detection at meat inspection; he suggested that the intramuscular route could be used for breeding animals.

In the studies now reported it is evident that cellular damage cannot be excluded, even though no visible reactions or lameness occurred in most of the animals after intramuscular injection. The fact that inspissated cysts and extensive fibrosis were sometimes found several months after intramuscular injection clearly indicates that this route should not be used.

The occasional large swellings occurring in the

brisket after subcutaneous injection, although unsightly, appeared to be of slight consequence. Sufficiently large numbers of all types and ages of cattle were used and kept under observation for 2 years after single and multiple injections to allow the conclusion that this route and site were otherwise satisfactory.

Increase in concentration of liver copper produced by a particular dose varied not only with the individual but also according to the route of injection, the initial copper status of the animal, and the type of feeding and management. Greatest increases were obtained in all age groups and types after intravenous injection of copper sulphate, but it appeared that the rate of fall, or depletion of liver copper, was more rapid after this method of administration than after subcutaneous or intramuscular injection of copper glycine. This finding is in agreement with observations made by Harvey (1959) on sheep.

Comparison of increases obtained after subcutaneous and intramuscular injections showed that greater increases almost always occurred after injection by the subcutaneous route. Although Cunningham (1957a) found a somewhat greater and less variable increase by the intramuscular route and concluded that it was, on the whole, more effective than the subcutaneous in increasing the copper content of the liver, his observations were made on relatively few animals of only one age group, *i.e.* yearling cattle, whose pre-injection liver copper values fell within the normal range.

It should be noted that repeated intramuscular injections of large doses of copper glycine into the three adult animals in the toxicity trial increased liver copper up to an apparent maximum, after which no further absorption appeared to occur.

Variation in uptake of copper by the liver appeared to be partly due to differences in feeding and management. Greater mean increases were obtained in housed animals on stall rations than in those of the same age group at grass, and comparison of grazing animals indicated that absorption was greater in those of normal copper status than those deficient in copper. In the herd deficient in copper, the post-injection samples of liver were all taken after an interval of 3 weeks, and therefore the lower values can perhaps be attributed to the rapid rate of depletion caused by the factor in the pastures "inducing" deficiency (Allcroft & Lewis, 1957), or they might be due to a lower uptake by liver cells whose metabolism had been changed by the "inducing" factor. Attention has already been drawn to the greater increase and absence of subsequent depletion occurring in housed animals on stall rations for a long period.

The evidence reported here shows that parenteral administration of copper to the dam, within 2 months of calving, increased the copper status of the newborn calf and that 120 mg. Cu as copper glycine is a safe dose for young calves. Although results are given only for calves 4 months old and upwards, doses of copper glycine supplying 120 mg. Cu have been given to calves of normal copper status from one month of age without any adverse effects.

It would thus appear that, in beef herds with symptoms of copper deficiency occurring in the calves from about 3 months of age, it would be beneficial to administer copper to the dam within a month or two of calving and to the calf at about 4 months of age. If the factor inducing deficiency is severe, the calf may need further injections at 4- to 6-month intervals. In dairy herds it would seem unnecessary to give copper to the dam before calving or to the calf while housed, but it may be necessary after turning the calf out to grass to give copper at about 6-monthly intervals until the animal comes into the milking herd and receives a concentrate ration in addition to grass.

In assessing the times at which doses of copper glycine should be given to beef calves deficient in copper, Cunningham (1957b) measured effectiveness of treatment in bringing animals to 15 months of age in a thrifty condition. He found that young calves 2 to 3 months of age could be safely injected and that best results were obtained by giving 3 injections, one at marking, one at weaning, and one 3 months after weaning. Further treatment of older animals was not always necessary; nevertheless, because of variation in severity of the condition from year to year and from farm to farm, Cunningham concluded that it was not possible to lay down any rule for treatment of adult beef animals and that injections should be given when necessary.

In the work on the duration of effect of injected copper, a lack of correlation was found between blood and liver copper levels. Blood copper levels in some groups were within the normal range, even though levels of liver copper were low. It is generally accepted that the concentration of copper in the liver provides the most reliable index of the animals' copper status, but Allcroft and Lewis (unpublished results) have observed that low blood copper levels usually occur only when the concentration of copper in the liver has been low for several months in animals grazing pastures on which an "induced" deficiency occurs. If a high molybdenum intake was the inducing factor, an elevated blood copper level would not be unexpected (Allcroft, 1952; Dick, 1954), but the pastures grazed by the copper-deficient herd on which the present observations were made had a molybdenum content of only 2 to 5 p.p.m., with a high copper content ranging from 15 to 37 p.p.m. (D.M.).

In an attempt to find a copper compound that would produce minimal reaction at the site of injection, give a good absorption of copper, and yet have a wide margin of safety, over 80 different compounds were investigated without success. The variations in reaction after injection into different species was notable. Some products gave no reaction in laboratory animals, but pronounced reactions in cattle. With copper glycine, however, the macroscopical appearance at the site of reaction in rabbits was similar to that in cattle. It was apparent that most copper compounds caused irritation and it seemed unlikely that one would be found that was non-irritant and would yet fulfil the other requirements. Copper glycine was the least unsatisfactory. The local reaction occurring after subcutaneous injection

(*Concluded at foot of page overleaf*)

Secondary, or False, Extrauterine Pregnancy in a Sow

BY

R. R. ASHDOWN and A. W. MARRABLE

Department of Veterinary Anatomy, The University, Bristol, 8

A SOW, which previously had produced litters of 10, 7, 1, 13 and 13 piglets, farrowed on March 20th, 1959, producing a singleton. Farrowing was uneventful and on the next 5 days the sow's temperature was 102·4, 102·4, 104·1, 103·1 and 102·4° F. Eleven extra piglets were transferred to the sow on March 21st but 8 died quickly. At weaning on May 21st the remaining piglets averaged 44 lb. The sow came on heat 48 hours after weaning and was served once by the boar. She was removed to a separate pen and remained there until slaughter on June 11th.

At slaughter a full term piglet was found in the peritoneal cavity. It lay in a thick caseous deposit, caudal to the stomach, with its back against the ansa spiralis of the colon. It was not covered by recognisable amnion but the foreparts were surrounded by thickened omentum which was adherent to the foetal head along the nasal septum. A mass of foetal membranes, still attached to the umbilicus, was firmly fused to the omentum. The flesh of the piglet was firm, neither mummified nor rotten. The skin was largely intact, though abraded over the bony prominences. In the dorsal wall of the right uterine horn there was a fistula, 5 cm. by 3 cm. in size, through which 2 lobes of swollen endometrium projected into the peritoneal cavity. The fistula lay in the cervical third of the horn and a 3 cm. slit in the dorsal layers of the broad ligament extended almost to the uterine fistula. The edges and surfaces of both holes were smooth and thickened. The right uterine horn was empty but in the cervical third of the left horn 2 normal embryos were found. These were 6 mm. long and clearly resulted from the service 19 days previously. The foetus found in the peritoneal cavity was 27.5 cm. long.

The obvious explanation of this case (which resembles that described by Benesch, 1934) is that uterine rupture occurred at the last farrowing and one piglet passed into the peritoneal cavity where it soon died. The uterine fistula was in process of healing and would probably have closed, leaving no trace of the path by which the foetus had left the uterus; the case would then have resembled that described by Schmidt (1957). It is remarkable that the maternal reaction to this occurrence was so slight; the piglet was probably out of the uterus for about 11 weeks yet, apart from local reaction in the omentum, there was no sign of peritonitis. The sow was never ill and conceived at the weaning heat. Ory (1946), Dozsa (1950) and Bertrand & Ferney (1954) have ascribed illnesses in cats to the presence of intra-peritoneal foetuses. Brauns (1942) recorded a case in which a piglet penetrated the ventral abdominal wall and was removed surgically. Acute peritonitis in a newly farrowed sow with a uterine fistula and 4 intra-peritoneal piglets was reported by Brixhe (1937).

Acknowledgments.—This case occurred in material generously given us by Cow and Gate Farms Ltd. Messrs. P. H. Sedgwick and P. Radford helped us; Mr. Sedgwick supplied the breeding history of the sow.

References

BENSCH, F. (1934). *Wien. tierärztl. Mschr.* **21.** 659-65.
BERTRAND, M., & FERNEY, J. (1954). *Bull Soc. Sci. vét., Lyon.* **56.** 39-41.
BRAUNS, K. (1942). *Berl. Münch. tierärztl. Wschr.* 1942. 336-7.
BRIXHE, P. (1937). *Ann. Méd. vét.* **82.** 416-7.
DOZSA, L. (1950). *Schweiz. Arch. Tierheilk.* **92.** 106-10.
ORY, J. (1946). *Rec. Méd. vét.* **122.** 71.
SCHMIDT, A. (1957). *Mh. Vet. Med.* **12.** 110-2.

Parenteral Administration of Copper Compounds to Cattle—*Concluded.*

into the brisket area was not severe enough to inconvenience animals under grazing or stall conditions and did not affect the milk yield. At 3 weeks after administration, copper storage was of the same order as that obtained after intravenous injection of copper sulphate, but the toxicity of parenterally administered copper glycine was much lower than that of copper sulphate. Its use also had the advantage of easily providing a controlled safe dose of copper, whereas supplementation in the food or as a mineral mixture provides uncertain and sometimes toxic amounts.

Acknowledgments.—We are grateful to Mr. K. N. Burns for his valuable assistance, and to Miss C. N. Hebert for statistical analysis of some of the data.

References

ALLCROFT, R. (1947). Unpublished observations.
———. (1952). *Vet. Rec.* **64.** 17.
———. (1957). *Ibid.* **69.** 785.
———, & LEWIS, G. (1954). Unpublished observations.
———, & ———. (1956). Proc. 7th Int. Grassland Congr., New Zealand. 377.
———, & ———. (1957). *J. Sci. Food Agric.* **8.** Suppl. Issue S96.
———, & PARKER, W. H. (1949). *Brit. J. Nutr.* **3.** 205.
CUNNINGHAM, I. J. (1946). *N.Z. J. Sci. Tech.* **27.** Sect. A. 381.
———. (1957a). *N.Z. Vet. J.* **5.** 9.
———. (1957b). *N.Z. J. Agric.* **95.** 218.
DICK, A. T. (1954). *Aust. Vet. J.* **30.** 197.
FIELD, H. I. (1957). *Vet. Rec.* **69.** 788.
GREEN, H. H. (1951). Proc. Specialist Conference in Agric., Australia, 1949. 293.
VAN DER GRIFT, J. (1955).) Diss. Utrecht.
HARVEY, J. M. (1959). Personal communication.
———, & SUTHERLAND, A. K. (1953). *Aust. Vet. J.* **29.** 261.
IAMIESON, S., & ALLCROFT, R. (1950). *Brit. J. Nutr.* **4.** 16.
———, & ———. (1951). Unpublished observations.
LOOSMORE, R. M., & ALLCROFT, R. (1951). *Vet. Rec.* **63.** 414.
MORGAN, D. E., & CLEGG, A. (1958). N.A.A.S. Quart. Rev. No. 41. P. 38. (London: H.M.S.O.)

Current Literature

ABSTRACTS

The 1958 Slaughterhouses Legislation: The Trade's Attitude. WHALLEY, J. B. (1959). *Sanitarian Lond.* **67.** 332.

The writer, who is the secretary of the National Federation of Meat Trades Associations, welcomes the Slaughterhouses Act because it has ended the period of uncertainty on the future pattern of slaughtering in England and Wales, and has given the trade the security it needed to justify expenditure on modernisation and new development. There is a "freedom period" which gives an opportunity for future planning, but this will not result in the opening of a large number of new slaughterhouses. Some old ones will disappear and some new ones will be built. In some places, as for example in Gainsborough and Newark, traders are combining to provide and share slaughterhouses. Small slaughterhouses will not be closed merely because of size, and the Minister can sanction new private licences even in restricted areas in certain circumstances.

Where local authorities have public abattoirs, the trade will require them to allow local butchers to slaughter their animals there.

The Federation is in agreement with the three main aims of the Act—hygienic conditions, humane treatment of animals, and safe working conditions for those working in slaughterhouses, and has suggested that its members discuss the interpretation of the Regulations with their local inspectors.

Regarding Regulation 5 of the Slaughter of Animals (Prevention of Cruelty) Regulations, which requires the provision of stunning pens, a slaughterhouse licence cannot be limited to one class of stock and the writer points out that although stunning pens do not have to be installed, it is an offence to slaughter adult cattle without using one. Special types of stunning pens are being made for the smaller slaughterhouses and local authorities are empowered to grant certificates of exemption for a limited time under specified conditions.

On the question of meat inspection, the Federation suggested in 1951 that an additional class of inspector should be authorised, the idea being not to replace the present qualified inspectors, but to supplement the work of the inspectorate. C. G. A.

Consideration of the Treatment and Prevention of Foreign Body Diseases in Cattle using Magnetic Instruments. ROSENBERGER, G., & STROBER, M. (1958). *Dtsch. Vier. Wockschrft.* **65.** 57, 98.

A tabular survey is given of previous authors' results using magnetic sounds and permanent magnets for the relief and prevention of traumatic reticulitis. Personal investigation concerned the use of 3 instruments: (a) Captometallsonde of del Seppia (Schubiger & Co., Lucerne); (b) Metall-Iraquator of Eisenhut, Basle; (c) Alnico permanent magnet of Cooper and Carroll. The authors' opinion is that the magnetic seekers (a) and (b) are not useful for the treatment of traumatic reticulitis for the following reasons. The damaging foreign body could (even with the additional help of the permanent magnet on 46 occasions up to now) only be removed in 10 cases out of 126 animals with the magnetic seeker. In the remaining animals a variable number of penetrating and loose foreign bodies were found. Of the 10 successes, 5 were then checked by rumenotomy; for economic reasons no operation was performed on the others. In using the seeker or sound the operator can unfortunately gain no impression of the condition of the abdominal organs, and therefore can take no necessary steps in supportive treatment or give an early judgment as to the economic value of the flesh if sent for casualty slaughter (20 out of 126 cattle).

The sick animals are endangered throughout the manipulative process by their uneasiness and frequent regurgitation of ruminal contents. (One experimental animal had to be slaughtered following aspiration pneumonia.)

It is unlikely that the development of stronger magnets and still more freely moveable seekers will reduce these disadvantages.

In careful prophylactic and diagnostic use the seekers are of value when combined with the permanent magnets. 32 out of 53 animals checked in this way, all with loose foreign bodies present, showed after treatment no positive signal using the electromagnetic metal detector. The widespread use of permanent magnets in America as a preventive for traumatic reticulitis is not without danger. The longer life-span of dairy cattle, damage to the mucous membrane, and the danger of indigestion are among points emphasised. Manual search of the reticulum in rumenotomy operations can be aided by use of the Alnico magnet. A.D.W.

A *Streptobacillus*, the Cause of Tendon-sheath Infection in Turkeys. BOYER, C. I., Jr., BRUNER, D. W., & BROWN, J. A. (1958). *Avian Diseases.* **2.** 418-27.

Streptobacillus moniliformis infection in man is usually associated with rat bites, constituting "rat-bite fever." Some cases show arthritis and joint swellings in addition to the fever.

The authors describe an outbreak of teno-synovitis in adult male turkeys. *S. moniliformis* was isolated from the one specimen examined. They were able to reproduce the disease in turkey poults but not in chicks. They attributed the outbreak to the heavy rat population on the farm in question.

***Salmonella* Organisms Isolated from Poultry Feed.** BOYER, C. I., Jr., BRUNER, D. W., & BROWN, J. A. (1958). *Avian Diseases.* **2.** 396-401.

Following an outbreak of *S. thomasville* infection in young turkey poults, examination of an unopened sack of the turkey food led to the isolation of the same organism. In view of this result the authors examined a further 33 samples of turkey starter mash. Five yielded Salmonella organisms belonging to 6 different serotypes. E. A. G.

A Successful Experimental Treatment of Brucellosis-infected Cattle with a New Drug (*short translated title*). (1958). *Dtsch. Tierarztl Wschr.* **65.** 257.

The drug Pecudin (N'-Dichloracetyl-N'phenyl-semicarbazid) was developed by Schraufstälter in the Bayer laboratories, Leverkusen, and has been found effective against brucellosis in mice and rats by Domagk. It was tested for its effectiveness against bovine brucellosis alone and when combined with Debenal-Bayer (Sulphapyrimidine). In the detailed experiments the authors successfully prevented brucellosis in artificially infected heifers. Since, for continuous treatment, Pecudin was as efficacious alone as in combination with Debenal, the main effect is attributed to Pecudin. Treatment began 8 days before artificial infection and was continued as permanent feeding at a dosage rate of 5 g. daily until calving. A heifer 2 months in calf, similarly infected 8 days following the commencement of Pecudin administration, also had a normal pregnancy, and this suggests the possibility of therapeutic action of the drug.

The treatment of infected animals in late pregnancy was unsuccessful in spite of high dosage levels, and the failure is attributed to the so-called placental barrier. During 6 months' observations no influence of Pecudin on the serological reactions of milk and blood or on the spread of Brucella in the milk could be shown. Suggestions are made for the use of the drug on farms acutely or subacutely infected and on those where there is the risk of the introduction of infection. By this treatment animals not yet infected should be protected, and infected heifers, either not, or less than 2 months in calf, may possibly be cured.

The authors anticipate that in Germany the use of Pecudin will considerably reduce losses from brucellosis, and that treated farms will be earlier certified as free from this disease.

Virus Abortion in Mares, and Equine Influenza (*translated title*). MANNINGER, R. (1958). *Dtsch. Tierarztl Wschr.* **65.** 369.

Equine influenza and so-called equine virus abortion are only different terms for an infection with the same virus. Depending on their resistance, naturally infected animals first show a more or less acute clinical picture of influenza after an incubation period of 3 to 7 days. Abortion follows in 18 to 59 days (other authors state 14 to 76 days) after infection. The preceding influenza stage, on account of its frequent mild course often remains unnoticed. Cross-immunisation, animal experiments, and the complement-fixation reaction, positive 10 days after infection, confirm the common identity of the viruses, which are considered responsible for 2 different diseases. It is difficult to control this disease in large studs Because pathological-anatomical and serological diagnosis depend on the aborted foetus, suspect animals among pregnant mares can only be recognised by daily temperature recording and by blood sampling for the complement fixation test before abortion occurs. A. D. W.

REPORT

Food Poisoning in England and Wales, 1958: A Report of the Public Health Laboratory Service. Monthly Bulletin of the Ministry of Health and the Public Health Laboratory Service (1959), October. Vol. 18. P. 169.

In 1958, 7,300 incidents of food poisoning were reported, an increase of 3 per cent. on 1957 but a decrease of 5 per cent. on 1956 and of 19 per cent. on 1955.

Of these incidents, 285 were general outbreaks, 601 family outbreaks, and 6,414 sporadic cases. Salmonellae were responsible for 28 per cent. of general outbreaks, 54 per cent. of family outbreaks, and 70 per cent. of sporadic cases. *Staphylococcus aureus* and *Clostridium welchii* were responsible for nearly all the remainder of incidents whose cause was known; the cause, however, was not discovered in 111 general oubreaks, 240 family outbreaks, and 1,893 sporadic cases.

Although at least 78 types of Salmonellae were incriminated in the different incidents of Salmonellae food poisoning reported, *Salmonella typhimurium* was responsible for about two-thirds of all of them. *Salmonella heidelberg*, almost unknown in this country a decade ago, has maintained its place, established in recent years, as the second most important food poisoning type; the source of this type still remains unknown.

Of the foods incriminated in outbreaks, processed or made-up meats maintained their important position, being responsible for 65 per cent. of the outbreaks attributed to specific foods. Of particular veterinary interest were 3 outbreaks of food poisoning associated with raw milk. Two were due to *S. typhimurium* and one to *Staph. aureus*. One of the *S. typhimurium* outbreaks was traced to a dairy worker who was an excreter of this organism and the other to 2 cows suffering from *S. typhimurium* enteritis. The *Staph. aureus* outbreak was traced by means of phage typing, to a cow suffering from acute Staphylococcus mastitis. A further 4 outbreaks of *Staph. aureus* food poisoning were due to the consumption of cheddar cheese.

The report stresses that salmonellosis continues to be by far the greatest problem of food poisoning in England and Wales and the need for control of known sources of the organisms responsible is urgent.

PROGRESS IN TWIN CALVING EXPERIMENTS

In a progress report made recently to the lay press, Dr. Joseph Edwards is stated to have said that though the experiments had been limited by many factors the outlook was encouraging.

The first cow having twins under this scheme calved successfully some weeks ago, and two other calvings were expected in the immediate future. It had been found that the technique could be grafted at any time on to any A.I. centre.

There was still much they hoped to learn, including the amount of hormone needed at the different seasons of the year.

At the request of the Editor of THE VETERINARY RECORD, a senior official of the Milk Marketing Board has undertaken to let us have an exclusive and more detailed progress report for publication in the near future.

News and Comment

THE QUEEN HONOURS THE ANIMAL HEALTH TRUST

At the annual meeting of the Trustees and Council of the Animal Health Trust, held at the Trust's headquarters last Wednesday, the Duke of Devonshire, honorary treasurer, deputising for the Duke of Norfolk, President of the Council, announced that the Queen had been graciously pleased to extend her Patronage to the Trust. Thus, after nearly 18 years of work in veterinary research and education, this voluntary organisation has achieved the highest honour open to such a body.

As most readers may know, Her Majesty has paid two unofficial visits to the Trust's Equine Research Station, and has donated for its use an electrocardiograph which was given to her on another occasion. Some of the Queen's own horses, and others belonging to the Queen Mother, have either been patients of the Station or have been examined there routinely while under training, so that the Royal Family are familiar with the important work done by Mr. William C. Miller, the director of the Equine Station, and his colleagues. It is hoped to quote some interesting notes on this work, not published widely hitherto, in our issue next week.

In the meantime, it is appropriate to observe that the honour accorded to the Animal Health Trust by the Queen is not less an honour to Dr. W. R. Wooldridge, the founder and Scientific Director of the Trust. He introduced that organisation in 1942, has played a principal part in guiding it through its formative years, and now is to be congratulated that the Monarch herself thinks fit to recognise formally the work of which he has been the principal architect. His colleagues, and many friends in the profession and outside it, will rejoice in the pleasure and deep satisfaction which he must feel.

TENTH BIRTHDAY OF "THE VETERINARY REVIEW"

A particularly enjoyable dinner party was held on October 30th at Charing Cross Hotel, to celebrate the tenth birthday of *The Veterinary Review*, a journal produced by Messrs. May & Baker. Mr. Paisley, a director of the company, whose special interest in veterinary matters has made him well known to, and widely popular with, members of the profession, was in the chair, and among the company were senior representatives of several veterinary schools, research institutes, the veterinary and scientific press, and general practice. The toast of the profession was proposed by Dr. W. R. Thrower and responded to by Mr. G. N. Gould, and that of the journal whose tenth birthday was being celebrated was proposed by the Editor of THE VETERINARY RECORD. Mr. Paisley's guests will look back upon a most harmonious and enjoyable evening.

ELECTION OF MEMBERS OF THE COUNCIL R.C.V.S.

In accordance with the provisions of the Veterinary Surgeons Act, 1948, five members of the said Council, who must be members of the Royal College, will be elected in 1960 by members of the Royal College residing outside the Republic of Ireland.

Five present members of Council will retire at the Annual General Meeting in 1960 and are eligible for re-election, namely:—

A. D. J. Brennan, C.B.E., M.R.C.V.S., Ministry of Agriculture, Hook Rise, Tolworth, Surbiton, Surrey; G. N. Gould, J.P., F.R.C.V.S., 10, Landguard Road, Southampton, Hampshire; P. S. Pugh, M.B.E., M.C., T.D., M.A., PH.D., M.R.C.V.S., A.R.I.C., Department of Veterinary Clinical Studies, Madingley Road, Cambridge; H. Sumner, C.B.E., M.V.SC., F.R.C.V.S., D.V.H., 16, Eaton Road, West Derby, Liverpool, 12; and H. M. Wilson, M.R.C.V.S., 134, Bonnygate, Cupar, Fife.

The term of office of the five persons elected in the place of the five members retiring by rotation will be four years.

Nominations of persons for election to the Council must be submitted in writing on a form which may be obtained from the undersigned, and which must be returned to him duly completed on or before January 31st, 1960.

Each such nomination form must bear the signature of the proposer and seconder, who must not be present members of Council, and must be countersigned by the nominee.

W. G. R. OATES, *Registrar.*
Veterinary Surgeons Acts, 1881-1948,
9, Red Lion Square,
London, W.C.1.

THE FULBRIGHT TRAVEL GRANTS

The United States Educational Commission in the United Kingdom announces that, under the provisions of the Fulbright programme, travel grants are available to citizens of the United Kingdom and dependent territories to go to the United States of America for academic or educational purposes, such as study, research, or lecturing. All awards are competitive and are made by the Board of Foreign Scholarships in Washington upon the recommendations of the Commission.

The basic criteria for the award of a travel grant are as follows:—

Graduate students. Applicants must hold by the time of departure, at least a good second-class degree or its equivalent and must show proof of admission to an institution of higher learning in the United States for a minimum period of nine months. Grants to graduate students are valid for a period of up to three years but are subject to annual renewal during this time.

Professors, lecturers, and senior research scholars should note that it is the objective of this programme that a maximum amount of time be

spent in the United States and, therefore, the Commission gives preference to those applicants who intend to spend a full academic year there. Of this, about two-thirds should be spent at one University or recognised research institution. Grants are not available for peripatetic visits or attendances at Conferences only. Grants may be extended up to a period of two years, subject to the continuance of satisfactory appointments and dollar support.

Those in the graduate student category are expected to go to the United States for the academic year beginning in September, 1960. For those in the lecturer/research scholar category, travel grants are available for those who are visiting the States between June 1st, 1960, and April 1st, 1961.

Since the funds of the Commission are in non-convertible sterling, it is not possible to offer grants for maintenance, tuition or incidental expenses within the United States.

The Commission reserves to itself the exclusive right to determine the validity of all qualifications presented to it and does not give reasons for its conclusions. There are two closing dates in this competition contingent upon the proposed departure date from the United Kingdom. They are:—

March 14th, 1960, for those travelling between June 1st, 1960, and August 15th, 1960.

June 1st, 1960, for those travelling between August 16th, 1960, and April 1st, 1961.

Those wishing to apply are first asked to fill up a record card. *This in itself does not constitute an application.* Full-length application forms are sent only when candidates indicate that their plans are complete—giving nature of appointment and dollar support available—which must be before the appropriate closing date. Full-length applications should be submitted *via* the Head of the candidate's College, University, or employing body. Applications should be made to: United States Educational Commission in the United Kingdom, 71, South Audley Street, London, W.1.

THE HAMPSHIRE CATTLE BREEDERS' SOCIETY

An announcement of considerable topical interest is made in the Society's current news bulletin as follows:—

National nominated service. The Milk Marketing Board and Private A.I. Centres throughout England, Scotland, and Wales have agreed to operate a national nominated service scheme from superior progeny tested sires standing at A.I. Centres throughout the country.

Any of the bulls shown on the list can, subject to supplies being available, be nominated by a member of any A.I. Centre, for the sum of £2 per first insemination.

This new scheme commenced on November 1st, 1959.

The list shows the contemporary comparison, butterfat percentage, and number of daughters of each bull. When studying the contemporary comparison, that is the average difference between the yields of the daughters of the bull and the daughters of other bulls milked in the same herds at the same time, due note should be taken of the number of daughters. Broadly, the higher the number of daughters the more reliable is the contemporary comparison.

Although eight of the Society's bulls are shown in the list, this does not affect the existing nominated service.

★

Solids-not-fat. A scheme is under consideration for the testing for solids-not-fat of a representative sample of heifers from each of the Friesian bulls standing at the Centre.

It is felt that although a correlation exists between butterfat and solids-not-fat, the knowledge obtained from the testing of A.I. progeny will assist in the better understanding of the problem. The method of taking samples and testing has not yet been worked out, but it is confidently expected that members will welcome the service and will be willing to co-operate.

THE R.C.V.S. TRUST

The council of the R.C.V.S. Trust announce the following fellowships and scholarships:—

The B.O.C.M. Fellowship for research in the field of animal husbandry, hygiene, and disease control in farm livestock, value £1,000 per annum.

The Cyanamid Research Fellowship for Studies in the Aetiology and Control of Bacterial Enteritis in Calves, value £1,000 per annum.

The Boots Research Scholarship in veterinary clinical medicine, value £750 per annum.

Further details, and application forms, may be obtained from the secretary, R.C.V.S. Trust, 9, Red Lion Square, W.C.1. The closing date for the receipt of applications is December 31st, 1959.

A.G.M. OF THE VETERINARY SECTION OF UFAW

The Annual General Meeting of the Veterinary Section of UFAW (the Universities Federation for Animal Welfare) was held at Knuston Hall, near Wellingborough, Northamptonshire, on Sunday, September 20th, 1959, and was addressed by the President-elect of the Section, Mr. T. Hughes Ellis, F.R.C.V.S., who spoke on "Some Painful Conditions in Animals and their Management." Mr. Hughes Ellis discussed the treatment, and more particularly the management, of a number of conditions frequently met with in practice. The importance and value of skilled treatment and good management in the early stages of illness he said could not be overstressed both from the point of view of minimising the pain suffered by the animal and of hastening its return to full health.

The meeting considered the following questions: the control of proprietary veterinary medicines, which it regarded as being of great importance to the welfare of animals requiring veterinary treatment; the appointment of veterinary surgeons as inspectors under the Pet Animals Act, 1951, which it urged; the use of rubber rings for castration, which it considered to be undesirable from both the humanitarian and the health aspects.

The attention of the meeting was drawn to the bad conditions prevailing in some broiler houses and it was suggested that legal minimum standards for poultry rearing by this method might be laid down. It was also reported that in some parts of the country there seemed to be a tendency to adopt the method of rearing calves in the dark, with restricted movement, to produce whiter flesh.

The following officers were elected: President, Mr. T. Hughes Ellis; President-Elect, Mr. Sydney Jennings; Honorary Secretary, Mr. John Volrath; and General Secretary, Miss M. P. Williams. Mr. Colin Pierrepoint of the University of Liverpool was elected as Student Chairman.

"THE INCISOR"

The Incisor, the magazine of the Students' Union Society of the Royal Veterinary College, is on sale at the College from November 5th. Its publication this year has unfortunately been delayed by the printing stoppage. The magazine contains a report of the opening of the College Field Station at Potters Bar by Her Majesty the Queen, an account of the Ninth A.V.S. Conference, and the President's Address, in addition to the usual complement of short stories, humour, cartoons, crossword, photographs, etc. It is regretted that the number of copies available is very limited.

PERSONAL

Mr. P. K. C. Austwick, of the Ministry of Agriculture, Central Veterinary Laboratory, Weybridge, has just returned from the 9th International Botanical Congress at Montreal, August 19th to 29th, and contributed a paper entitled "Morphology of Dermatophytes" to a symposium on ringworm fungi. In Canada visits were made to the Canadian Department of Agriculture, Research Branch, and Animal Diseases Research Laboratory at Ottawa, and to the Ontario Veterinary College at Guelph, where he attended a seminar on animal mycoses. Subsequently a tour was made of 15 Government establishments, universities, and hospitals in the United States engaged in veterinary and medical mycological research.

Births

GRIME.—On October 18th, to Anne, wife of Philip Ayrton Grime, M.R.C.V.S., of Windsor, Berkshire, a daughter, Charlotte Louise.

HALL.—On October 17th, 1959, to Barbara, wife of Leslie Hall, M.A., B.SC., PH.D., M.R.C.V.S., a son, Nicholas, brother for Michael.

Marriages

BOSWOOD—MARTIN.—On Saturday, October 31st, 1959, at Rugby, Warwickshire, Bryan Boswood, B.A., VET.M.B., M.R.C.V.S., to Janet E. M. Martin, B.A.

PRIZE-WINNING ENTRY IN I.V.C., PHOTOGRAPHIC COMPETITION

This composite photograph, illustrating how one of the malpostures encountered in bovine obstetrics is corrected, won a prize in the photographic exhibition which formed part of the International Veterinary Congress. It was submitted by Mr. P. R. Greenough of Castle Cary, Somerset, a member of the B.V.A.

EAGLESOME—HOWIE.—At Dunlop Kirk, on October 31st, 1959, by the Rev. A. Dunn, M.A., B.D., assisted by the Rev. A. Easton, Matthew D. (Bobby) Eaglesome, B.V.M.S., M.R.C.V.S., only son of Mr. and Mrs. Matt. Eaglesome, 46, Irvine Road, Kilmarnock, to Edith S. D. Howie, M.S.R.(R), only daughter of Mr. Andrew L. Howie, Netherhouses, Dunlop.

MARR—CLEGG.—At Sevenoaks, on October 10th, 1959, Alfred Marr, B.SC., PH.D., M.R.C.V.S., to Rosemary, daughter of Mr. and Mrs. R. C. Clegg, Appleton Hall, Montego Bay, Jamaica.

COMING EVENTS

November

11th (Wed.). General Meeting of the Lancashire Veterinary Association at Liverpool, 2.30 p.m.

Meeting of the Southern Counties Veterinary Society at the Royal Hotel, Winchester, 7.30 p.m.

12th (Thurs.). Special Meeting followed by an Ordinary General Meeting of the Central Veterinary Society at the Royal Veterinary College, Camden Town, N.W.1., 6 p.m.

13th (Fri.). Annual General Meeting of the North Wales Division at the Gwydyr Hotel, Bettws-y-Coed, 2 p.m.

General Meeting of the Midland Counties Veterinary Association at Chateau Impney, Droitwich, 2.30 p.m.

22nd Commemoration Ball of the Royal Veterinary College in the Great Hall, 8 p.m.

18th (Wed.). Meeting of the Scottish Metropolitan Division in the Royal (Dick) School of Veterinary Studies, Edinburgh, 2.30 p.m.

Dinner-Dance of the Western Counties Veterinary Association at the Imperial Hotel, Exeter, 7 p.m.

19th (Thurs.). Annual Dinner-Dance of the V.V.B.F. Northern Region in the Northern Hotel, Aberdeen, 7.30 p.m.

Meeting of the Society of Practising Veterinary Surgeons at the Royal Station Hotel, York, 7.30 p.m.

Annual Dance of the V.V.B.F. County of Ayr Ladies' Guild in Western House, Ayr.

Reception and Dance of the Shropshire Veterinary Club at the Grapes, Bicton Heath, Shrewsbury, 9 p.m.

Dinner-Dance of the Lakeland Veterinary Association at the Hydro Hotel, Windermere, 7.30 p.m.

20th (Fri.). Dinner-Dance of the V.V.B.F. Ladies' Guild, Dumfries and Galloway Division, in Lockerbie House Hotel.

25th (Wed.). Annual Supper Dance of the Scottish Metropolitan Division at the Calton Hotel, North Bridge, Edinburgh, 8 p.m.

26th (Thurs.). Meeting of the B.V.A. Overseas Committee at 7, Mansfield Street, London, W.1, 11 a.m.

Meeting of the Supplementary Veterinary Register Association at 7 Mansfield Street, Portland Place, London, W.1., 2 p.m.

27th (Fri.). Annual Dance of the Northern Ireland Veterinary Association in Thompson's Restaurant, Callender Street, Belfast, 11.30 p.m.

28th (Sat.). Meeting of the Metropolitan Region of the B.S.A.V.A. at 1, Wimpole Street, London, W.1; dinner 7 p.m. for 7.30 p.m.; paper 9 p.m.

December

6th (Sun.). Meeting of the Kenya Veterinary Association at Uplands Bacon Factory and Sports Club, 11 a.m.

ADDRESSES OF DISEASE INFECTED PREMISES

The list given below indicates, first the county in which are situated the premises on which disease has been confirmed, followed by the postal address and date of outbreak.

Anthrax

Ayr. Milncraig Farm, Coylton; West Whitelees Farm, Stewarton, Kilmarnock (Oct. 27); Ralstonhill Farm, Hurlford, Kilmarnock (Nov. 2).

Ches. Malcoff Farm, Chapel-en-le-Frith, Stockport (Oct. 27).

Devon. Holbrook Farm, Honiton Clyst, Exeter (Oct. 28); East Down Farm, Blackawton, Totnes (Oct. 30).

Dumfries. Penlaw Farm, Lockerbie (Oct. 29).

Fowl Pest

Beds. Park Farm, Bromham (Nov. 1).

Bucks. 193, Aylesbury Road, Bierton, Aylesbury (Oct. 28).

Berwick. Bridge Haugh Mill, Earlston (Oct. 27).

Cambs. 6, The Avenue, March (Oct. 30); 13, Field Baulk, March (Nov. 1); 24, Field Baulk, March (Nov. 2).

Gloucs. Shardlow, North Road, The Reddings, Cheltenham (Oct. 29); Glebe Cottages, Chasleton, Moreton-in-Marsh; Golden Cross, Stretton-on-Fosse, Moreton-in-Marsh (Oct. 31).

Hunts. Gore Lodge Poultry Farm, Goretree Road, Hemingford Grey (Oct. 28); C13 Holding, Homefield Road, Chawston, St. Neots (Oct. 31).

Kent. Springette Hill Farm, West Malling; 9 and 10, Arcady Manor Way, Belvedere (Oct. 31); 31, Mill Road, Erith; 62, North Road, Belvedere (Nov. 1).

Lancs. 8, Farnworth House Estate, Duxbury, Chorley (Oct. 31).

Lincs. 18, Manor Street, Ruskington, Sleaford; Cocks Farm, High Street, Ruskington, Sleaford (Oct. 31); 34, Manor Street, Ruskington, Sleaford; Glen Gorring Poultry Farm, Fen Road, Ruskington, Sleaford (Nov. 1); Hartswood Farm, Lincoln Road, Ruskington, Sleaford (Nov. 2).

London. The Stables, Crossfield Street, Deptford, S.E.8 (Oct. 27).

Norfolk. Calthorpe, Erpingham, Norwich; Pear Tree Farm, Wreningham, Norwich; 4, Council House, Calthorpe, Erpingham (Oct. 29); Highfields, Swanton Morley, Dereham; Tower House Allotments, Erpingham, Norwich (Oct. 30); Mardle Farm, Tivetshall, Norwich (Oct. 31); 32, Wier Avenue, Mattishall, Dereham (Nov. 1).

Roxburgh. Elm Cottage, Maxton, St. Boswells; Eastfield, Bowden, St. Boswell (Oct. 27).

Selkirk. Easter Essenside Cottages, Ashkirk (Oct. 28); Blainslie, Galashiels (Oct. 29).

Suffolk. Felsham Hall, Felsham, Bury St. Edmunds (Oct. 27); Mausoleum Farm, Felsham, Bury St. Edmunds (Nov. 1); Frog Hall, Felsham (Nov. 2).

Surrey. 37, Salcot Crescent, New Addington (Oct. 27); Garlands Farm, Ewhurst, Cranleigh (Oct. 28); Wyvenhoe, Guildford Road, Bookham, Leatherhead (Nov. 1).

Sussex. Morgan Farm, Rushlake Green, Heathfield (Oct. 29); Antve Farm, Theobalds Road, Burgess Hill; Inglenook Smallholding, Battle Road, Westham, Pevensey (Oct. 30).

Warwick. Gooseberry Hall Farm, Barford (Oct. 31).

Worcs. 13, Bredon Vale, Broadway Lane, Fladbury, Pershore; Acton Farm, Stourport-on-Severn (Oct. 31); Down Rip Farm, Hinton-on-the-Green, Evesham; No. 1, South View, Wyre, Pershore (Nov. 1).

Letters to the Editor

The views expressed in letters addressed to the Editor represent the personal opinions of the writer only and their publication does not imply endorsement by the B.V.A.

The Control of Swine Fever

Sir,—We have recently received, no doubt with many others, a circular on swine fever from the Ministry of Agriculture. This seems to me to be a tremendous improvement on previous ones, and is obviously very helpful to farmers. I am not so sure that the same applies to veterinary surgeons: it seems to make an outbreak so easy to control. Is this the case? Are there any practical records for the control of swine fever and if so where are they published? Indeed is there any work of this sort being carried out and if so by whom?

Disease control experiments of these kinds seem to me to be basic and even vital, but there appear to be very many different solutions, often not based on controlled research. Mr. Steele-Bodger's recent letter on Johne's disease seems to cover much the same point. I would like to ask, Sir, through your columns, if the B.V.A. can initiate or influence practical research on such subjects. The results would be invaluable to me for one.

Yours faithfully,

Glasgow House, R. M. S. NEAVE.
5, Chapel Street, Colchester.
October 27th, 1959.

Public Relations and the Profession

Sir,—I am pleased to see that a Professional Secretary has now been appointed to serve the B.V.A. Judging by the events of the past few weeks his time should be fully occupied. Let us hope that his most urgent task will be to enter into correspondence with the B.B.C., who would seem to be unaware of the existence of the Association. On television last week we were treated to a lengthy interview with a gentleman describing himself as a canine psychiatrist, complete with staff, hospital, and tranquillisers. At the end of the interview a passing reference was made to the profession, a woman stating that she preferred to take her animal to a psychiatrist rather than a "vet" as the treatment of mental illness in animals was hardly within the province of the latter!

Close on the heels of this effort came the story of the rejected bull, later to be given the full treatment in the press. The description of the castration of this animal, complete with two operators and overalled "nurse," called forth the most scathing comments I have yet heard from my farmer friends. If the profession is not to be brought into ridicule something must be done, and done soon, to improve our relations with the B.B.C. and the press.

A far more serious matter, which has caused a great deal of anxiety in many quarters, is the question of conditions of importation of monkeys for poliomyelitis vaccine production. In a recent journey from Singapore to Rotterdam by boat some 125 out of 300 animals were found to have died when the ship called at a British port. It is essential that these animals be used, and this being the case, surely, at any rate as far as British vaccine-producing firms are concerned, these firms have a duty to ensure that the monkeys are humanely transported by air only. Presumably these firms have veterinary surgeons on their staffs who could supervise dispatch from Singapore and if necessary travel with the animals. We are not told how these animals are trapped in India, but this is a question which also appears to warrant a searching enquiry.

Yours faithfully,

Manor House, HAROLD L. SMITH.
Rowde, Devizes.
October 31st, 1959.

The Colonial Veterinary Service

Sir,—Finance is often a primary consideration in determining whether to take a post overseas, and therefore I should be interested to know why in some cases the initial salary offered is only a few pounds above the minimum figure below which a veterinary officer could not expect to live comfortably.

A veterinary officer under these conditions could not expect to save sufficiently for any unforeseen emergency. What then?

Yours faithfully,

NORMAN S. M. MACLEOD.

33, College Road,
Framlingham, Suffolk.
October 30th, 1959.

An Emergency Locum Service

Sir,—On a very foggy night last November I was telephoned by the wife of a veterinary surgeon whose practice was 180 miles from mine. Her husband, a single-handed practitioner and a personal friend of mine, had been knocked down by a bull and taken to hospital with suspected concussion. The problem was, who would look after his practice until he was fit again?

I was quite unable at such short notice to find a locum, and so I motored down myself and held the fort for about 7 days

It was brought home to me very forcibly that there must be many occasions similar to this when help is urgently needed and not forthcoming.

My partners and I have now decided to run a pilot scheme to see if an emergency locum service is required at this time. We are inserting an advertisement in THE VETERINARY RECORD this week offering this service subject to our availability, and trust the idea will prove acceptable to the profession.

The terms we are quoting initially are in line with those being offered for tuberculin testing in Eire and are, we think, sufficiently high to ensure that only genuine emergencies will warrant our use. It is not our normal intention to act as locums for holidays or for periods of any great length, but rather to act as temporary help until other arrangements can be made.

Yours faithfully,

Derwent, V. A. HARRISON.
Church Street, Matlock.
November 1st, 1959.

Pharmacological Effects of Suxamethonium

Sir,—The article by Neal and Wright (THE VETERINARY RECORD, October 17th, 1959) draws attention to a most important effect of succinylcholine (suxamethonium) chloride on the cardiovascular system of the conscious horse. They report the occurrence of tachycardia and arrhythmias and their findings are confirmed by Tavernor (THE VETERINARY RECORD, October 24th, 1959) who also records 2 cases of cardiac arrest associated with the use of suxamethonium. Recent experimental studies carried out in this Department concerning the side-effects produced by suxamethonium throw further light on these clinical observations.

In horses under thiopentone-cyclopropane/oxygen anaesthesia, the intravenous injection of suxamethonium chloride in doses of 0.17 mg. per kg. bodyweight has been found to cause a rise of about 50 mm. of mercury in the systolic blood pressure without producing apnoea. The injection of 0.34 mg. per kg. has caused a rise of over 100 mm. of mercury in both the systolic and diastolic pressures. These doses have produced increases in the pulse rate of about 30 and 125 per cent. respectively. When phenothiazine derivatives, which have both adrenolytic and anticholinergic properties, are used for premedication the blood pressure response consists of an initial fall followed by a small rise.

This observation suggests that in anaesthetised horses the injection of suxamethonium causes stimulation of post-ganglionic autonomic nerve fibres and a release of adrenaline from the adrenal medulla. Such stimulation of autonomic nerves and release of adrenaline has, in fact, already been demonstrated in anaesthetised dogs and cats (Thesleff, 1952; Hummell, 1958; Stevenson, 1959). Since it is generally agreed that the production of these effects by any agent can provoke cardiac irregularities there is probably no need to postulate that in horses suxamethonium may have a direct effect upon the cardiac centre or the heart muscle as was suggested by Hansson (1958). Furthermore, it is unlikely that asphyxia plays any part in the production of these phenomena for the increase in blood pressure and pulse frequency were seen in horses which were breathing a mixture containing 80 per cent. of oxygen in a closed circuit with efficient carbon dioxide absorption. However, there is one other explanation of the cardiac disturbances which must be considered.

In one horse the administration of 0.34 mg. per kg. of suxamethonium was shown to cause a slow depolarisation of the surface of the external vastus muscle. The depolarisation potential reached a peak of 5 mV within 2 minutes of injection of the drug and returned to zero after a further 12 minutes. In the cat and dog similar changes in muscle potential are associated with a marked increase in the plasma potassium concentration and in the urinary excretion of potassium (Paton, 1956; Stevenson, 1959). In 2 ponies the administration of 0.15 mg. per kg. of suxamethonium chloride has been shown to increase the plasma potassium concentration by as much as 3 m.equiv./l (Stevenson, 1957). An increase of this magnitude may well be sufficient to embarrass cardiac function or cause cardiac arrest.

It is clear from the reports of other workers and the experimental findings recorded here that the use of suxamethonium for casting horses is not unassociated with risk to the life of even healthy animals.

Yours faithfully,

D. E. STEVENSON,
L. W. HALL.

Department of Veterinary Clinical Studies,
School of Veterinary Medicine,
University of Cambridge.
October 30th, 1959.

Reference

HANSSON, C. H. (1958). *Nord. Vet. Med.* **10.** 201.
HUMMELL, P. R. (1958). *Curr. Res. Anaes.* **37.** 130.
PATON, W. D. M. (1956). *Brit. J. Anaes.* **28.** 470.
STEVENSON, D. E. (1957). Unpublished observations.
———, (1959). In press.
THESLEFF, S. (1952). *Acta. Physiol. scand.* **27.** Suppl. 99.

DISEASES OF ANIMALS ACT, 1950—GREAT BRITAIN
Summary of Returns of Confirmed Outbreaks of Scheduled (Notifiable) Diseases

Period		Anthrax	Atrophic Rhinitis	Foot-and-Mouth	Fowl Pest	Sheep Scab	Swine Fever
1st to 15th Oct., 1959		15	1	—	70	—	58
Corresponding period in	1958	13	—	1	47	—	36
	1957	13	1	30	48	—	37
	1956	15	2	11	41	—	38
1st Jan. to 15th Oct., 1959		196	2	9	610	—	983
Corresponding period in	1958	132	5	115	584	—	1,026
	1957	270	7	94	668	—	764
	1956	1,161	10	127	557	—	630

TUBERCULOSIS (ATTESTED HERDS) SCHEMES

The number of Attested Herds, *i.e.*, herds officially certified as free from Tuberculosis as at 30th September 1959, was as follows :—

ENGLAND	WALES	SCOTLAND	TOTAL (GREAT BRITAIN)
148,838	38,472	44,046	231,356

TUBERCULOSIS ORDER OF 1938

The number of bovine animals slaughtered under the Tuberculosis Order of 1938 during the period 1st July to 30th September, 1959, was 25.